UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,790	01/14/2002	Richard A. Rosenbloom	QUIG-1006CIP	3053

21302 7590 04/30/2004

KNOBLE, YOSHIDA & DUNLEAVY
EIGHT PENN CENTER
SUITE 1350, 1628 JOHN F KENNEDY BLVD
PHILADELPHIA, PA 19103

EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,790	ROSENBLOOM, RICHARD A.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 8, 2003, September 2, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 8, 2003.

This Office Action is a response to Applicant's request for continued examination (RCE) filed October 8, 2003, and amendment and response to the Final Office Action (mailed March 26, 2003), filed September 2, 2003 wherein claims 1-20 have been amended. Currently, claims 1-20 are pending in this application.

Claims 1-20 are examined on the merits herein.

The declaration of Dr. Anthony W. Addison (not inventor) submitted September 2, 2003 under 37 CFR 1.132, is acknowledged and will be further discussed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, and 12-19 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular compounds effective to regulate at least one of cell differentiation and cell proliferation such as vitamin D3, the particular antioxidants such as vitamin A, vitamin E or coenzyme Q10, the particular anti-inflammatories disclosed in the specification employed in the particular method of treatment of radiation injury herein, does not reasonably provide enablement for any substances or compounds represented by "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation", "one or more antioxidants" and "anti-inflammatories" recited in the claims herein.

These recitations, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation", "one or more antioxidants" and "anti-inflammatories", are seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to the particular method of treatment of radiation injury herein comprising active agents herein.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since the claims reads on any compounds represented by "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation", "one or more antioxidants" and "anti-inflammatories".

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A

definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation", "one or more antioxidants" and "anti-inflammatories" recited in the instant claims are purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides those particular compounds for each kind of functional compounds in the specification).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).
The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the

genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a human) the ***combination*** of any compounds represented by "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation", "one or more antioxidants" and "anti-inflammatories", which especially broadly encompass those known and unknown compounds that regulate at least one of cell differentiation and cell proliferation, those known and unknown antioxidants and anti-inflammatories as of the instant filing date, as well as those future known compounds. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can

have significant adverse consequences" (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having claimed functional properties in the pharmaceutical compositions herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that the Examples 1-3 of the specification at page 23-27 provide merely those particular compounds for each kind of functional compounds the instant compositions. Thus, the evidence in the examples is not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed composition. See MPEP § 716.02(d).

Thus, the specification fails to provide sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations employed in the claimed compositions to be administered to a host, with no assurance of success.

Applicant's remarks and the declaration of Dr. Anthony W. Addison filed September 2, 2003 regarding the rejection of claims 1-20 made under 35 U.S.C. 112, first paragraph for lack of scope of enablement have been fully considered but are unpersuasive. These remarks are believed to be adequately addressed by the rejection under 35 U.S.C. 112, first paragraph set forth above.

Additionally, it is noted that this rejection is made under 35 U.S.C. 112, first paragraph for lack of scope of enablement, **not** made under 35 U.S.C. 112, first paragraph for lack of "Written Description". Thus, Applicant's argument in the remarks and declaration regarding the "Written Description Guideline" has been considered but not convincing.

In response to the list of the anti-inflammatory drugs approved by FDA in Applicant's argument and Exhibit L, note that the instant claims are not limited to those

anti-inflammatory drugs approved by FDA and those known antioxidants and antioxidant enzymes as discussed above.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 7, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations, “analogs”, “may be”, “other”, "derivatives" in the claims render claims 2-3 and 7 indefinite. The recitations, “analogs”, “may be”, “other”, "derivatives" of various kinds of compounds are not clearly defined in the specification. Since one of ordinary skill in the art would clearly recognize many various groups possibly substituting these compounds, any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physiological effects and functions. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to “analogs”, “may be”, “other”, "derivatives" of various kinds of compounds encompassed thereby.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 and 12-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent 09/993003, allowed and being issued.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to the same method of the treatment comprising the same active agents as the claims of the instant application. Thus, these methods between in the patent and in the instant application are seen to substantially overlap.

Thus, the instant claims -9 and 12-20 are seen to be anticipated by the claims 1-11 of the allowed 09/993003.

Claims 1, 4-9, and 12- 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application No. 10/288,761.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to the same method of the

treatment comprising the same active agents as the claims of the instant application. Thus, these methods between in the copending application and in the instant application are seen to substantially overlap.

Thus, the instant claims 1, 4-9, and 12- 20 are seen to be obvious over the claims 1-40 of copending Application No. 10/288,761.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 4-9, and 12- 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 10/279,315.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a method for the reduction or treatment of reactive and inflammatory dermatoses comprising the same active agents as the claims of the instant application. One of ordinary skill in the art would recognize that radiation injury in a patient would be reactive and inflammatory dermatoses. Thus, these methods between in the copending application and in the instant application are seen to substantially overlap.

Thus, the instant claims 1, 4-9, and 12- 20 are seen to be obvious over the claims 1-25 of copending Application No. 10/279,315.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over KITA, K (WO 9718817, equivalent to 6,162,801), and Bissett et al. (of record) and Darr et al. (of record) in view of Shimoi et al. (of record) and Kim et al. (5,776,460, of record).

Kita discloses that vitamin D including vitamin D3 (cholecalciferol), is useful in a dermatological composition for the protection and treatment of the skin and scalp from harmful UV radiation. See 6,162,801, abstract, col.1 lines 22-24 and 51-67, col.4 lines 13-16, and col.8 lines 51 to col. 9.

Bissett et al. discloses that an antioxidant alone such as vitamin C (asorbic acid), or in combination with an anti-inflammatory agent are useful in treating UV radiation-induced chronic skin damage in a mammal. See abstract, page 86 1st paragraph, and Discussion in page 90.

Darr et al. discloses that vitamin C such as asorbic acid or vitamin E is useful in a composition to be administered orally or topically in the treatment of the protection of UV radiation-induced damage. See Summary and page 247.

The prior art does not expressly disclose the employment of the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for

the treatment or reduction of radiation injury. The prior art does also not expressly disclose the composition herein further comprising flavonoid / flavonoid derivatives, and ginseng.

Shimoi et al. discloses that flavonoid / flavonoid derivatives from plant or tea are antioxidants and have radioprotective effects. See abstract.

Kim et al. discloses that ginseng is known to be useful in the protection of radiation injury. See col.1 lines 21-27.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for the treatment or reduction of radiation injury, and to further comprise flavonoid / flavonoid derivatives, and ginseng in the claimed method.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for the treatment or reduction of radiation injury since vitamin D such as vitamin D3 is known to be useful for the protection and treatment of the skin and scalp from harmful UV radiation. Antioxidants such as vitamin C (asorbic acid) is known to be useful in the treatment and the protection of UV radiation-induced damage. Moreover, ascorbyl palmitate is a known vitamin C (an ester of asorbic acid). Therefore, one of ordinary skill in the art would have reasonably expected that combining vitamin D3 and ascorbyl palmitate known useful for the same

purpose, i.e., treating radiation damage, in a composition to be would improve the therapeutic effect in treating radiation injury.

Further, both flavonoid / flavonoid derivatives and ginseng are known antioxidants and also known to be useful in the protection of radiation injury. Therefore, one of ordinary skill in the art would have reasonably expected that further adding both flavonoid / flavonoid derivatives and ginseng to the composition herein known useful for the same purpose, in a composition to be administered would provide additive effects for the therapeutic treatment in radiation injury.

Since all active composition components herein are known to useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed September 2, 2003 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons.

Applicant asserts that Kita dose not teach a vitamin D to be administered orally in the claimed method herein in treating radiation injury in a human. Contrary to

Applicant's assertion, Kita teaches that "Therapeutic vitamin D is administered orally or by injection, and is applied to the skin as an active vitamin D ointment in the case of skin conditions" (see col.1 lines 42-44 in particular). Kita further teaches that "It is known that the molecular structure of vitamin D is altered in the liver and kidneys, converting it into biologically active vitamin D" (see col.1 lines 44-46 in particular), and "It is now known that there are active vitamin D receptors in the cells, and the inhibition of cell activity is being studied since active vitamin D inhibits the production of a variety of cytokines" (see col.1 lines 63-67). Moreover, Kita teaches that "In general, the ultraviolet (UV) light absorption spectra of vitamin D and active vitamin D have absorption maxima 265 nm, with the molar absorption coefficients of about 18,000". See col.1 lines 25-28. Hence, one of skill in the art would recognize that the molar absorption coefficients of UV radiation for vitamin D are very high. Therefore, based on the teachings of Kita, one of ordinary skill in the art would have found it obvious to administer a vitamin D orally in treating radiation injury in a human.

Additionally, oral administrations of vitamin D are well-known in the art. Thus, oral administration of vitamin D would inherently treat radiation injury in a human under the doctrine of inherency. See *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001).

Furthermore, as indicated in the previous Office Action, since all active composition components herein are known to useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects

would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

It is noted that the record contains no clear and convincing evidence of nonobviousness or unexpected results for the oral compositions herein employed in the claimed method herein over the prior art.

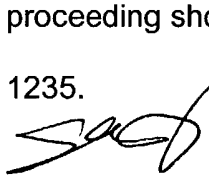
For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is 571.272.0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on 571.272.0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.



S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
April 22, 2004